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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,774	10/14/2003	Richard S. Dondero	CELL-0276	3355

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,774	DONDERO ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-20* is/are pending in the application.

4a) Of the above claim(s) *1-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 11/30/06 to the non-final action of 6/1/06 is acknowledged.

Claims 1-6 and 8-20 are pending.

Claims 1-6 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 8-20 are examined on the merit.

Any objections and rejections not specifically mentioned here is considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/01143 of Pillai, et al., in view of US 5,286,847 issued to Gehrke, et al and further in view of Beissert, et al., The Journal of Investigative Dermatology, 1998, 111,609-615 as stated in our previous office action dated 1/6/06.

In the instant application, applicants claim a method of modulating immune response of a subject to a vaccine antigen comprising administering an effective amount of IL-1 mutein having reduced toxicity, in concurrent or sequential combination with said vaccine antigen.

Applicants state that the primary reference does not teach a method that comprises an interleukin-1 mutein (reiterating the examiner's statement that the primary reference is deficient in not using the interleukin mutein). Applicants argue that Gehrke patent discloses a mutant IL-$1\beta_{Arg127\text{-}Gly}$ mutant that exhibited decreased biological activity as compared to native, mature IL-1β polypeptide in a thymocyte costimulation assay (Figure 2) and that $1\beta_{Arg127\text{-}Gly}$ mutant bound the IL-1 receptor as efficiently as the native, mature IL-1β polypeptide (Figure 3). The patent further states that the mutant can act as an IL-1β inhibitor by binding to IL-1 receptors and interfering with the binding of native IL-1β (col. 3, lns 55 to 59). The patent explains that the mutant can thus be used as an "anti-inflammatory, anti-immune agent" for the treatment of autoimmune diseases caused by the excessive or unregulated action of IL-1, such as rheumatoid arthritis, osteoarthritis, and gouty arthritis (col 4, lns 27 to 31 and lns 39 to 45), and therefore, the

Gehrke patent teaches away from the use of mutant as an adjuvant by being an anti-immune agent. Applicants further argue that Beissert article does not teach or suggest the using an IL-α or IL-1β mutein having reduced toxicity as adjuvant. Therefore, a person skilled in the art would not be motivated to combine the teachings of Pillai, Gehrke and Biessert because Gehrke patent teaches away from its combination with other two references specifically patent teaches that the IL-$1\beta_{Arg127\text{-}Gly}$ mutant exhibited reduced biological activity relative to native IL-1β, but fails to teach or suggest that the mutant possesses immuno-stimulatory and immuno-enhancing activities comparable to those of native IL-1β. For the same reason, one skilled in the art would not have reasonably expected that the IL-$1\beta_{Arg127\text{-}Gly}$ mutant described in the Gehrke patent would have been useful as a vaccine adjuvant.

Applicant's arguments filed 11/30/06 have been fully considered but they are not persuasive. Because, applicants are claiming a method of **modulating immune response of subject to a vaccine antigen** administering an effective amount of IL-1 mutein having **reduced toxicity** in concurrent or sequential combination with vaccine antigen (emphasis added by examiner). Applicants in their arguments appears to be focused on the fact that Gehrke reference teaches that IL- $1\beta_{Arg127\text{-}Gly}$ disclosed in the reference shows high receptor binding activity and reduced biological activity and the mutant can be used as an anti-inflammatory or anti-immune agent for the treatment of autoimmune diseases caused by the excessive or unregulated action of IL-1 because the IL-1β mutein of Gehrke binds to the IL-1 receptor. It should be noted that the present claims are drawn to **modulating immune response** and **not** for **primarily increasing immune response** to the administration of **vaccine antigen** and **not to** the **administration of**

IL-1 mutein (IL-1 mutein is an adjuvant). The dictionary meaning of the word 'modulate' according 'http://dictionary.cambridge.org/define.asp?key=modulate*1+0&dict=A' is 'vary the strength, quality or amount of something'. Thus, even if the IL-1β mutein of Gehrke reference has reduced biological activity and lower immune response, it still meets the limitations of the claim. Therefore, the reference of Gehrke does not teach away from the instant claimed invention. With regards to applicant's comment on Beissert's reference, it should be noted the reference was used to show that prior treatment of Langerhans cells with IL-1α or IL-1β induces differential tumor immunity to S1509a tumor associated antigens and the adjuvants and the antigens can be administered in a sequential combination.

Therefore, the rejection as stated in our office action dated 1/6/06 under 35 USC 103 is proper and maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

2/1/09
ANISH GUPTA
PRIMARY EXAMINER

Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654